Clinical characteristics and outcomes of hepatitis B virus carriers infected with COVID-19 at the Jinyintan hospital in WuHan, China

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Abstract

Background: Coronavirus 2019 (COVID-19) is a novel infectious disease that was earliest reported in Wuhan, China, but has been later discovered everywhere in the world. On the other hand, Hepatitis B virus (HBV) is ubiquitous in China; having millions of HBV carriers, HBV infection has become a major problem of public health in China. In this study, we aim to describe the clinical features of HBV carriers infected with COVID-19 and to assess factors that may affect the progression and outcome of the disease.

Methods: 72 patients diagnosed as infected with both COVID-19 and HBV at the Jinyintan Hospital of Wuhan have been involved in this study. Epidemiological characteristics, demographic features, clinical manifestations, laboratory test, treatment, management and final outcomes of these patients were collected and analyzed.

Results: Among all 72 patients (40 male and 32 female, with a median age of 58.5 years old), 22 (30.56%) were diagnosed as severe cases and 50 (69.44%) non-severe cases. Fever is the most common symptom, followed by cough, chest tightness and sputum. Significant differences have been observed in the outcomes of laboratory tests including hematologic, biochemical, infection and coagulation parameters, and in indicators like Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Total Bilirubin (TBil), Direct Bilirubin (DBil), Indirect Bilirubin (IBil) and γ-glutamyl Transferase (GGT) at the admission and discharge of these patients. Especially, levels of Prealbumin (PA) and Serum Amyloid A (SAA) showed an obvious trend of decreasing, which is statistically significant.

Conclusions: The clinical features of HBV carriers infected with COVID-19 have obvious systemic symptoms, such as fever, cough, and chest tightness. By comparing their liver functions tested on the dates of admission and discharge, we found that the SARS-CoV-2 virus, which causes COVID-19, does not directly activate the Hepatitis B virus, so that the risk of liver cell damage for HBV carriers infected with COVID-19 does not increase. Both PA and SAA seem to work as sensitive indicators and can be used to evaluate the prognosis and outcome of these patients.

Background

In December 2019, a new type of pneumonia of unknown pathogen was discovered in Wuhan, Hubei Province, China. Its clinical manifestations are very similar to viral pneumonia [1]. Through deep sequencing analysis on the lower respiratory tract samples of the patients, the virus that caused such a disease was named as SARS-CoV-2 [2], and the corresponding disease COVID-19. According to the interim guidelines of the World Health Organization (WHO), the diagnosis of COVID-19 mainly depends on a nucleic acid test of SARS-CoV-2 in respiratory specimens.

A Hepatitis B virus (HBV) carrier is a person who is chronically infected with hepatitis B virus and tests positive for hepatitis B surface antigen (HBsAg) for more than 6 months. HBV carriers rarely have liver-related symptoms or signs, and their liver functions are normal. After analyzing the clinical features of 72 HBV carriers diagnosed with COVID-19 at Wuhan Jinyintan Hospital, this study aims to clarify the clinical

characteristics of HBV carriers infected with COVID-19 and find out possible factors that may affect the outcomes.

Methods

Study design & subjects

Jinyintan Hospital, a specialist hospital of infectious diseases in Wuhan, undertook the treatment of most COVID-19 patients in Wuhan during the epidemic from January to April 2020. Among these COVID-19 patients, some are hepatitis B virus carriers (HBV antigen positive on admission). Hepatitis B virus carriers must meet the HBsAg (+) and HBeAg (-). All patients were HBV carriers and diagnosed with COVID-19, according to the interim guideline of the World Health Organization (WHO) [3]. In this paper, we conducted a study on 72 such patients admitted between January 10 and February 24, 2020. Epidemiological characteristics, clinical manifestations, laboratory test results, CT scan imagings and clinical treatments of these patients were collected from their electronic medical records.

Some patients are recognized as severe cases by any of the following conditions [4]: 1) A significant increase in respiratory rate (≥30 times/min); 2) Oxygen Saturation ≤93%; 3) Partial pressure of oxygen(PaO2)/fraction of inspired oxygen(FiO2) ≤300 mmHg; or 4) Respiratory or other organs failure that requires intensive care unit (ICU) monitoring and treatment or shock.

Liver test abnormality was defined by elevations of the following liver enzymes in serum: ALT>35U/L, AST>40U/L, GGT>45U/L, alkaline phosphatase (ALP)>135U/L and TBil>21umol/L. As COVID-19 is a new infectious disease, guidelines on liver injury classification is not yet available. Therefore, we define ALT and/or AST >3 upper limit units (ULN), ALP, GGT, and/or TBil >2 ULN as criteria for liver injury [4].

Most clinical data used in this study were collected from the day of admission to the day before discharge. Written informed consent was waived for the retrospective case series and it would not cause any potential risk to any patient.

Statisitical analysis

Descriptive analysis of variables is expressed as median (interquartile range [IQR]) or percentage (%). When the data are normally distributed, an independent group t-test is used to compare the means of continuous variables. Otherwise, a Mann-Whitney test is used. For the classified variables, Chi-squared test (x^2-test) was conducted. All analysis were performed using SPSS version 23.0, and p value <0.05 is considered statistically significant.

Results

3.1 Basic information of the patients

All 72 HBV carriers with confirmed COVID-19 admitted to the Jinyintan Hospital, including 40 males and 32 females, were involved in this study (Table 1). Ages of these patients range from 27 to 82, with a median 58.5 years old, and about 37.50% of the patients are over 65 years old. As for the A-B-O blood group, blood type A came out to be the majority (38.89%).

Table 1. Basic information of the patients

Study population	No.(%)
No. of patients	72
Ages, median(IQR), y	58.5 (27-82)
⩾65	27 (37.50)
<65	45 (62.50)
Gender	
Male	40 (55.56)
Female	32 (44.44)
ABO blood group	
A	28 (38.89)
B	10 (13.89)
AB	10 (13.89)
O	19 (26.39)
UK	4 (5.56)
Disease duration (d)	
Date of illness onset to hospital admission	15 (4-32)
Date of illness onset to nucleic acid turning negative	22 (16-25)
Date of hospital admission to discharge	12 (9-15)
Clinical manifestation	
Fever(T⩾37.3℃)	64 (88.89)
Cough	61 (84.72)
Sputum	44 (61.11)
Chest tightness	46 (63.89)
Shortness of breath	31 (43.06)
Diarrhea	17 (23.61)
Fatigue	35 (48.61)
Anorexia	42 (58.33)
Sore throat	1 (1.39)
Chest pain	2 (2.78)
Loss of sense of taste and smell	1 (1.39)
Comorbidities	
Hypertension	24 (33.33)
Diabetes	11 (15.28)
Coronary heart disease	7 (9.72)
Liver cirrhosis	1 (1.39)
Others	7 (9.72)
Classification	
Severe cases	22 (30.56)
Non-severe cases	50 (69.44)
Chest imaging	
Unilateral	5 (6.94)
Bilateral	67 (93.06)
Treatment in hospital	
Oxygen therapy	
Nasal cannula	58 (80.55)
HFNC	9 (12.50)
NPPV	4 (5.56)
IPPV	1 (1.39)
Methylprednisolone	17 (23.61)
Medicine Therapy	
Antibiotic	63 (87.50)
Antiviral	57 (79.17)
Clinical outcomes	
Recovery	69 (95.83)
Death	3 (4.17)

Except where indicated, data=n/N (%), n is number of patients, where N is the total number of patients with available data.

The median time from onset to medical treatment for these patients was 15 days, and on average it took 22 days for their nucleic acid tuning negative. Fever (88.89%) was the most common symptom, followed

by cough (84.72%), chest tightness (63.89%), sputum (61.11%), anorexia (58.33%), fatigue (48.61%), and shortness of breath (43.06%). 17 patients (23.61%) had gastrointestinal symptoms, such as diarrhea. Few patients (1.39%) lost sense of taste and smell. Many patients had comorbidities, including hypertension (n=24, 33.33%), diabetes (n=11, 15.28%), coronary heart disease (n=7, 9.72%) and cirrhosis (n =1, 1.39%).

22 (30.56%) patients had respiratory failure and were considered as severe cases upon admission. Chest CT imaging showed that 67 patients (93.06%) had infection on bilateral lungs. Most patients required oxygen support in the hospital, including nasal intubation (n=58, 80.55%), high-flow nasal intubation oxygen therapy (HFNC) (n=9, 12.50%), non-invasive positive pressure ventilation (NPPV) (n=4, 5.56%) and invasive positive pressure ventilation (IPPV) (n=1, 1.39%). Most patients received empirical antibiotic treatment (n=63, 87.50%) and anti-virus treatment (n=57, 79.17%). 17 (23.61%) patients received methylprednisolone with a total dose ranging from 40 mg per day to 160 mg per day. After treatment, 69 patients recovered and 3 patients died; the death rate is 4.17%.

3.2 Indicators of laboratory liver tests at admmision

Most patients were with HBsAg (+) and HBeAg (-). 39 patients (54.17%) were abnormal in liver function tests and 9 (12.50%) had liver injury, including hepatocellular (ALT, AST) and cholestatic abnormalities (ALP, GGT). Upon admission, numbers of patients who have increased ALT, AST, TBil, ALP or GGT were 29 (40.28%), 22 (30.56%), 7 (9.72%), 1 (1.39%) and 20 (27.78%) respectively (Table 2).

Table 2. Indicators of laboratory liver tests at admmision

	Admission
No.(%)	72
HBV type	
HBsAg (+) and HBeAg (+)	3 (4.17)
HBsAg (+) and HBeAg (-)	69 (95.83)
Liver function in admission	
normal	33 (45.83)
abnormal	39 (54.17)
Abnormality type	
Hepatocellular	4 (5.56)
AST>3LN	2
ALT>3LN	4
Cholestatic	7 (9.72)
ALP>2LN	0
GGT>2LN	7
Mixed	9 (12.50)
ALT, U/L	
Normal	43 (59.72)
1-2 ULN	21 (29.17)
2-3 ULN	4 (5.56)
>3 ULN	4 (5.56)
AST, U/L	
Normal	50 (69.44)
1-2 ULN	18 (25.00)
2-3 ULN	2 (2.78)
>3 ULN	2 (2.78)
TBIL, umol/L	
Normal	65 (90.28)
1-2 ULN	5 (6.94)
2-3 ULN	2 (2.78)
>3 ULN	0 (0.0)
ALP, U/L	
Normal	71 (98.61)
1-2 ULN	1 (1.39)
2-3 ULN	0 (0.0)
>3 ULN	0 (0.0)
GGT, U/L	
Normal	52 (72.22)
1-2 ULN	13 (18.06)
2-3 ULN	4 (5.56)
>3 ULN	3 (4.17)

Except where indicated, data=n/N (%), n is number of patients, where N is the total number of patients with available data.

A majority of the patients presented mild liver abnormalities. Additionally, 4 patients who had liver injury presented >3 ULN elevation of ALT, 2 patients presented >3 ULN elevation of AST and 3 patients presented >3 ULN elevation of GGT.

3.3 Contrasts in indicators of laboratory tests between admission and discharge

All patients received blood test, virology test and chest CT examination at their first visit. Some of these tests or examinations are required to be redone before discharge. Table 3 shows a contrast between the laboratory test indicators for all patients when they were admitted and discharged. In blood tests, no significant difference has been observed, including white blood cell count(WBC)、neutrophilic granulocyte(NE)、lymphocyte(LY)、eosinophil(EO)、platelets(PLT) , as well as neutral lymphatic ratio (NLR). However, some indicators of the liver function, including AST, GGT and lactate dehydrogenase (LDH), show observable trends of improvement for all patients before discharge than at admission. Albumin (ALB) is significantly increased, and so is the Albumin globulin ratio. At admission most patients were found to have a significantly lower level of PA than normal, but during the treatment their PA levels gradually recovered to a normal range as their conditions were improved ($P<0.001$). SAA and serum ferritin have shown a declining trend in this study ($P<0.05$), while other infections and coagulation function indexes did not change much before and after the treatment ($P>0.05$). The INR of most patients only slightly increased ($P<0.05$).

Table 3. Contrasts in indicators of laboratory tests between admission and discharge

	Reference values	Admission Value, median(IQR)	Discharge Value, median(IQR)	P 值
Hematologic				
WBC, x10°/L	3.5-9.5	4.87 (4.15-6.98)	5.82 (4.16-7.04)	0.49
NE, x10°/L	1.8-6.3	3.45 (2.51-4.98)	3.7 (2.41-5.20)	0.89
LY, x10°/L	1.1-3.2	1.04 (0.75-1.48)	1.25 (0.96-1.48)	0.27
EO, x10°/L	0.02-0.52	0.04 (0.01-0.07)	0.09 (0.03-0.18)	0.07
PLT, x10°/L	125-350	201 (155-251)	225 (179-299)	0.13
NLR	NA	3.28 (2.09-5.52)	3.04 (1.69-5.44)	0.19
Biochemical				
TBil, umol/L	0-21	12.6 (10.03-17.05)	9.85 (6.90-13.28)	0.00#
DBil, umol/L	0-8	4.2 (3.15-5.48)	2.85 (1.80-4.13)	0.00#
IBil, umol/L	0-13	8.8 (6.5-11.72)	7.2 (4.43-9.28)	0.00**
AST, U/L	7-40	32 (25-46.50)	24.5 (18.75-36.25)	0.00*
ALT, U/L	13-35	30.5 (20-51.75)	32.5 (18.75-52.25)	0.11
TP, g/L	65-85	64.2 (60.40-68.8)	67.4 (62.30-71.48)	0.00#
ALB, g/L	40-55	32.05 (29-34.88)	35.75 (30.50-39.43)	0.00#
Globulin, g/L	20-40	31.35 (29.28-34.95)	31.5 (29.20-35.18)	0.93
Prealbumin, mg/L	180-350	105.5(67.50-168.25)	191 (124-233)	0.00#
A/G	(1.2-2.4):1	1.0 (0.90-1.18)	1.1 (0.90-1.30)	0.00#
ALP, U/L	50-135	73.5 (59.25-85.75)	65 (57.00-85.00)	0.18
GGT, U/L	7-45	27 (20.00-51.75)	24.5 (17.75-46)	0.05
TBA, umol/L	0-12	4.2 (2.55-7.75)	4.4 (2.40-7.10)	0.23
LDH, U/L	120-250	269 (228.50-356.50)	228 (188-250)	0.06
Infection indics				
hs-CRP, mg/L	0-5	27.15 (5.65-89.38)	8.05 (1.83-31.28)	0.09
CRP, mg/L	0-6	54.25(13.23-253.58)	1.9 (1.10-3.20)	0.06
IL-6, pg/L	0-7	9.58 (7.26-12.94)	8.52 (6.71-11.17)	0.54
ESR, mm/h	0-20	39.2 (25.50-58.0)	39 (24.50-109.00)	0.10
SAA, mg/L	0-10	173.7 (43.14-278.2)	11.53(2.39-105.4)	0.00#
PCT, ng/mL	NA	0.05 (0.00-0.11)	0.05 (0.05-0.33)	0.23
Serum ferritin, ng/mL	4.63-204	450.32(258.51-794.24)	358.79(223.49-592.30)	0.00**
Coagulation function				
PT, s	10.5-13.5	11.4 (10.60-12.28)	11.6 (10.90-12.10)	0.06
APTT, s	21-37	26.3 (22.25-31.28)	25.2 (23.60-28.30)	0.52
INR	0.8-1.2	0.98 (0.91-1.07)	1.0 (0.94-1.06)	0.02*
D-dimer, ug/mL	0.21	0.63 (0.39-1.15)	0.77 (0.24-2.40)	0.39
PT-Fbg, g/L	2-4	4.15 (3.20-5.28)	2.9 (2.50-4.70)	0.21
CEA, ng/mL	0-5	3.05 (1.45-4.95)	UK	NA
AFP, ng/mL	0-13.4	1.75 (1.36-2.73)	UK	NA

*P<0.05, **P<0.01, #P<0.001.

Discussion

COVID-19 has become a global public health crisis, with as many as 4 million reported cases of infection, in which 84,431 cases are in China. Meanwhile, a total of 300 million people in the world have been infected with hepatitis B (HBV) as of March 2018, while the number of HBs-Ag positive people in China is about 86 million [5].

Liver is an organ located between the portal vein and the systemic circulation. It is often exposed

potentially to viruses, bacteria and inflammatory, which may sometimes cause liver damage. It is reported that people infected with SARS [6] and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) [7] had liver damage. A recent epidemiological study in Wuhan showed that of the 99 patients initially infected with 2019-nCoV, 43 had varying degrees of liver dysfunction and their ALT or AST were both above the normal level [8]. In another retrospective analysis of the patients of COVID-19 with impaired liver function, it was also found that abnormal liver function was common in patients with COVID-19 [9]. A meta-analysis showed that the incidences of abnormalities in ALT, AST and TBil were 29%, 22.7% and 11.7% respectively [10]. Pathological findings have revealed that the liver biopsy specimen of patients died of COVID-19 were moderate microvesicular steatosis and mild leaflets, with portal vein activity, indicating that SARS-CoV-2 may cause liver damage [11]. Viral RNA was also detected in liver tissues in concentrations exceeding viremia [12].

For HBV carriers, it is unclear whether SARS-CoV-2 will exacerbate liver function damage or not. Few studies have analyzed the clinical characteristics and outcomes of hepatitis B virus carriers complicated by COVID-19. In this study, we investigated 72 HBV carriers infected with COVID-19, among whom 39 (54.2%) had abnormal liver examination results, and 9 (12.50%) had liver injury upon admission. With the treatment of COVID-19, their liver function indicators gradually returned into normal ranges. The above result is similar to a recent retrospective study based on the characteristics of liver function tests in large hospitals [4], which reported that about half of the COVID-19 patients also had abnormal liver function, and about 5% of them had liver injury upon admission. It is suggested that among the carriers of hepatitis B, the incidence of liver function damage may not increase.

Some studies have shown that patients with abnormal liver functions will encounter a higher risk of serious illness [4]. However, in our study, we found that only for few patients abnormal liver functions had actually exacerbated the disease and caused liver damage. This finding is consistent with the results of another retrospective study showing that despite liver function abnormalities are common in patients with COVID-19, liver damage is not the main feature of COVID-19 and may not have serious clinical consequences [9]. SARS-CoV-2 can directly attack the liver and cause liver dysfunction, but as far as we concern, it should be distinguished from the liver function damage caused by the inflammatory factor storm that may be related to the aggravation of the disease.

Two recent studies have shown that angiotensin converting enzyme 2 (ACE2) is a key receptor for SARS-CoV-2 [13] [14]. RNA-seq data in the Human Protein Atlas (HPA) database [15] shows that ACE2 is relatively of low expression in liver and lung, which are the main target organs for 2019-nCoV and SARS. A Low-throughput study of ACE2 protein expression in the liver indicates that ACE2 occurs infrequently in cholangiocytes, but does not occur at all in hepatocytes, Kupffer cells, and endothelial cells [16]. A near recent study [17] found that coronavirus may directly bind to ACE2-positive cholangiocytes, but not necessarily to hepatocytes, indicating that liver abnormalities in SARS and COVID-19 patients may not be caused by hepatocyte damage, but induced probably by cholangiocyte dysfunction or other causes, such as drug toxicity and systemic inflammatory response. However, after analyzing the indicators of abnormal liver function at the time of admission, we found that there were not only cholangiocyte

dysfunction, but also hepatocyte damage, suggesting that for hepatitis B carriers, in the early stage of COVID-19, SARS-CoV-2 may directly attack hepatocytes as well as cholangiocyte. Therefore, in addition to ACE2, whether there are other SARS-CoV-2 binding sites on hepatocytes, such as CD147 [18], DC-SIGN and l-sign [19] remains to be further clarified. Meanwhile, it is not ruled out that the liver dysfunction in these patients is due to coronavirus-induced inflammation or drug toxicity.

Severe and/or critical patients had a significantly higher pooled incidence of abnormal liver biochemical indicators at admission than mild and/or moderate patients [20]. In this study, we found sensitive prognostic indicators. A majority of the patients had a significantly lower levels of PA when they were admitted, but their PA levels can gradually recover to normal before rehabilitation or discharge: the difference between their PA levels at admission and discharge was statistically significant ($P<0.0001$). PA is an acute reactive protein and mainly present in the blood and cerebrospinal fluid; its plasma half-life is around 1.9 days. PA is synthesized in the liver. When liver damage occurs and intrahepatic synthesis decreases, it can be quickly detected through a decrease of the PA level in peripheral blood at an early stage. Therefore, it is considered to be a sensitive indicator of liver function damage and recovery. Our results show that compared to other liver function indicators, the early dynamic changes of PA can be used as a more sensitive indicator to judge the prognosis and outcomes of HBV carriers complicated with COVID-19.

Our research also conducted an exploratory analysis of infection-related indicators. We found that levels of SAA of the patients increased at an initial stage and will gradually return to normal after recovery. SAA is also an acute phase protein and is commonly used to assess the acute response process; similar expression can also be found in serum ferritin.

It is well known that there is a dynamic balance between HBV and the host immune system. When the balance is broken, HBV cccDNA is the main substance that replicates with HBV in hepatocytes, which will speed up the replication, increase the number of infected cells, and cause HBV reactivation to a certain extent [21]. Therefore, treatmentsthat may impair immune response, such as tumor chemotherapy, immunosuppression or transplantation, may cause HBV reactivation. COVID-19 is also associated with immune imbalances, while peripheral blood neutrophils are significantly increased and lymphocyte counts are significantly decreased [22] [23] [24]. Therefore, in this study, we tried to explore whether SARS-CoV-2 can cause HBV activation in HBV carriers. Generally, the diagnosis of HBV activation is based on dynamic monitoring of HBV DNA quantitative detection and liver function (especially ALT). However, based on retrospective analysis and limited laboratory test data, there is no direct evidence that SARS-CoV-2 may cause hepatitis B virus reactivation [25]. From the patients' prognosis and recovery of liver function, SARS-CoV-2 does not seem to directly cause HBV reactivation. In addition, the inflammatory cytokine storm is thought to be related to the severity of the disease, so large doses of glucocorticoids and immunosuppressants are often recommended during the treatment. In this condition, whether it will reactivate HBV and aggravate the occurrence of liver function damage remains to be further studied.

Our study has certain limitations. First of all, due to the design of this retrospective study, we had limited number of cases in a single hospital and not all patients have undergone full laboratory tests, especially liver tests and HBV-DNA quantitative detection. Second, since most patients have had a good prognosis and only three patients died, the potential impact of liver abnormalities or injury on mortality cannot be well assessed. With the emergence of new cases of COVID-19 on HBV carriers throughout the world, it will be necessary to conduct further studies with more data.

In summary, this study describes the clinical features of HBV carriers infected with COVID-19. We found that more than half of the patients had varying degrees of liver dysfunction in an early stage of the pneumonia, but these abnormalities can be gradually cured during the treatment. This phenomenon may be due to SARS-CoV-2 directly attacking hepatocytes and cholangiocytes. Both PA and SAA are sensitive indicators and can be used to judge the prognosis and outcome of the patients. In addition, in this study, we did not find direct evidence that SARS-CoV-2 may cause hepatitis B virus reactivation. Further study is still needed to explore the impact of SARS-CoV-2 on hepatitis B carriers.

Conclusions

Clinical features of HBV carriers with COVID-19 have obvious systemic symptoms. Liver function data on admission and discharge of these patients suggested that SARS-CoV-2 does not seem to directly activate the Hepatitis B virus, and the risk of liver cell damage of HBV carriers with COVID-19 does not increase. PA and SAA may be are sensitive indicators to evaluate the prognosis and outcome of the patients.

List Of Abbreviations

ACE2: angiotensin converting enzyme 2; AFP: a-fetoprotein; ALB: albumin; ALP: alkaline phosphatase; ALT: alanine aminotransferase; APTT: activated partial thromboplastin time; AST: aspartate aminotransferase; CEA: carcino-embryonic antigen; CRP: C-reactive protein; DBil: direct bilirubin; ESR: erythrocyte sedimentation rate; EO: eosinophil; GGT: γ-glutamyl transferase; HBV: hepatitis B virus; HbsAg: hepatitis B surface antigen; HBVM: HBV serologic marker; HFNC: high flow nasal cannula oxygen therapy; HPA: human protein atlas; hs-CRP: high-sensitivity C-reactive protein; IBil: indirect bilirubin; ICU: intensive care unit; IL-6: interleukin-6; INR: international standard ratio; IPPV: invasive positive pressure ventilation; IQR: interquartile range; LDH: lactate dehydrogenase; LY: lymphocyte; MERS-CoV: Middle East respiratory syndrome coronavirus; NE: neutrophilic granulocyte; NLR: Neutral lymphoid ratio; NPPV: noninvasive positive pressure ventilation; PCT: Procalcitonin; PLT: platelets; PT: prothrombin time; PT-Fbg: Fibrinogen; SAA: serum amyloid A; TBA: total bile acid; TBil: total bilirubin; TP: Total protein; ULN: upper limit units; WBC: white blood cell count; WHO: World Health Organization;

Declarations

Ethics approval and consent to participate

The ethics committee of Wuhan Jinyintan Hospital approved this study and granted a waiver of informed consent from study participants (KY-2020-42.01).

Written informed consent was waived for the retrospective case series and it would not cause any potential risk to patients.

Consent for publication

Not applicable.

Availability of data and materials

All the data supporting used in this work were publicly available.

Competing interests

The authors declare that they have no conflict of interests.

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Authors' contributions

The first draft of the manuscript was produced by JJL, MH, XZ, HZ, FLW, JHH, ZLG, QL, QY and ZFY.

JJL, QL and QY were major contributors in the conception and design of the study, analysis and interpretation of data. MH, XZ and ZFY were major contributors in acquisition of data. HZ, FLW and JHH were major contributors in drafting the article. ZLG and QL revising the article.

All authors reviewed, edited, and approved the final versions of the submitted manuscript.

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